FILE 'PROMT' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'INPADOC' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'USPATFULL' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'PCTFULL' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'GENBANK' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'IMSDRUGNEWS' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'NLDB' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'ABI-INFORM' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'BIOSIS' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'BIOTECHDS' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'EUROPATFULL' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'IFIPAT' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'PHIN' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'TOXCENTER' ENTERED AT 20:24:40 ON 14 AUG 2004

FILE 'WPIDS' ENTERED AT 20:24:40 ON 14 AUG 2004

=> s e4b9
L4 11 E4B9

=> d que
L4 11 SEA E4B9

=> d l4 bib ab kwic 1-11

L4 ANSWER 1 OF 11 PROMT COPYRIGHT 2004 Gale Group on STN

AN 2000:284538 PROMT

TI VE-cadherin-2 antagonists, ImClone Systems ImClone Systems preclinicaldata.
SO R & D Focus Drug News, (17 Apr 2000) .
ISSN: 1350-1135.
PB IMS World Publications Ltd.
DT Newsletter
LA English
WC 106
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB At the 91st annual meeting of the American Association for Cancer Research, 1-5 April 2000, San Francisco, USA, ImClone Systems presented results from its program which aims to identify monoclonal antibody antagonists of vascular endothelial cadherin, with potential use in the treatment of cancer. The monoclonal antibody **E4B9** inhibited adherens junction formation with negligible disruption of existing junctions in vitro. The antibody also demonstrated the ability to block angiogenesis in a mouse corneal pocket assay. A company spokesperson told R&D focus that studies are ongoing to determine efficacy of the antibody in tumor models.
THIS IS THE FULL TEXT: COPYRIGHT 2000 IMS World Publications Ltd.
At . . . to identify monoclonal antibody antagonists of vascular endothelial cadherin, with potential use in the treatment of cancer. The monoclonal antibody **E4B9** inhibited adherens junction formation with negligible disruption of existing junctions in vitro. The antibody also demonstrated the ability to block. . .
TX At . . . to identify monoclonal antibody antagonists of vascular endothelial cadherin, with potential use in the treatment of cancer. The monoclonal antibody **E4B9** inhibited adherens junction formation with negligible disruption of existing junctions in vitro. The antibody also demonstrated the ability to block. . .
VE-cadherin-2 antagonists, ImClone Systems, **E4B9**, L1X, Other

L4 ANSWER 2 OF 11 USPATFULL on STN
AN 2002:287144 USPATFULL
TI Antibody antagonists of VE-cadherin without adverse effects on vascular permeability
IN Liao, Fang, New York, NY, UNITED STATES
Hicklin, Daniel J., Glen Ridge, NJ, UNITED STATES
Bohlen, Peter, New York, NY, UNITED STATES
PI US 2002160003 A1 20021031
AI US 2002-40128 A1 20020102 (10)
RLI Continuation of Ser. No. US 2000-540967, filed on 31 Mar 2000, ABANDONED
DT Utility
FS APPLICATION
LREP KENYON & KENYON, ONE BROADWAY, NEW YORK, NY, 10004
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 1119
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to antibodies, or immunologically active fragments thereof, specific for the N-terminal 15 amino acids of a mammalian VE-cadherin and which act as antagonists of VE-cadherin-mediated homophilic interactions between adjacent endothelial cells without adversely affecting normal vasculature. In a preferred embodiment, the antibodies are humanized antibodies directed that react with human VE-cadherin for use in a human. The invention also

provides pharmaceutical compositions comprising these antibodies and antibody fragments, methods of preparing the antibodies, and methods of using the antibodies and antibody fragments to inhibit angiogenesis, inhibit tumor metastasis, or treat cell proliferative disorders.

SUMM . . . antibodies. Likewise, preferred antibody fragments are from monoclonal antibodies. In a more preferred embodiment, the monoclonal antibody is monoclonal antibody **E4B9**. The preferred mammal of the invention is a human.

DRWD [0030] FIG. 4: Antibody **E4B9** does not exhibit significant effect on paracellular permeability. Antibodies **E4B9** and 6D 10 do not exert dramatic effect on vascular permeability.

DRWD [0031] FIGS. 5A & 5B: Antibody **E4B9** exhibits potent anti-angiogenesis activity in mouse corneal micropocket assay. Three representative eyes from each experimental group (6 mice/group) are tested. Antibody **E4B9** possesses >80% inhibitory activity on corneal neovascularization.

DRWD [0032] FIG. 6: Antibody **E4B9** cross-reacts with human VE-cadherin.

DRWD [0035] FIG. 9: Predicted epitope region for antibody 19E6 and 10G4. The underlined regions are the epitopes for antibodies **E4B9** and Cad-5, respectively.

DETD . . . angiogenesis in vivo or in vitro or inhibit tumor metastasis. The preferred antibody of the invention is murine monoclonal antibody **E4B9**.

DETD . . . of the invention includes the hybridomas which produce monoclonal antibodies of the invention. One such hybridoma producing rat anti-murine VE-cadherin **E4B9** has been deposited with the ATCC, Rockville, Md. and assigned accession number _____.

DETD . . . known in the art, a humanized version of non-human antibodies can be prepared. for example a humanized version of monoclonal **E4B9** can be readily prepared by cloning the gene encoding this antibody in to an appropriate expression vector. Useful the nucleic. .

DETD . . . "permeability" assays to examine their new junction formation inhibiting activity and existing junction disrupting activity, respectively. Among these 20 antibodies, **E4B9** was shown to specifically inhibit adherens junction formation without adversely affecting normal vasculature (FIGS. 3 and 4). Furthermore, the **E4B9** antibody was also tested in an in vivo angiogenesis assay and showed greater than 80% inhibition of corneal neovascularization (FIG.. . . .about. 2 VEC switch Assay Permeability

MAb.sup.1	(Blot)	(Blot)	(IF)	(% Increase)
19E6.sup.2	+	+	+	120 .about. 50
6D10	+	+	+	20
E4B9 (P1).sup.3	+	+	+	<20
E4G10 (P1)	+	+	+	<20
E3F2 (P2)	+	-	-	<20
1F6.1 (P2)	+	-	-	<20

10E4.1. . . bacterially-expressed protein containing extracellular domains 1 and 2 of the N-terminus of murine VE-cadherin; IF, immunofluorescence.

.sup.2Control antibody.

.sup.3This antibody, **E4B9**, cross-reacts with human VE-cadherin.

DETD . . . +++ +++

BV6	Domain 3	+++	+++
TEA	Domain 4	+/-	+/-
Hec1.2	Domain 4	-	-

				Toxicity
Anti-murine VEC				
19E6	Domain 1	+++	+++	+
E4B9	Domain 1	+/-	+++	-
10G4	Domain 1	ND	+++	ND
6D10	Domain 3-4	+/-	+/-	-

.sup.1See Table 1.

DETD **E4B9** Crossreacts with Human VE-Cadherin

DETD [0094] The murine epitope sequence recognized by antibody **E4B9** (peptide 1) shares 100% homology with human VE-cadherin, so this antibody was examined to determine if it cross-reacts with human VE-cadherin. Western-blot analysis of several VE-cadherin expressing human and murine cell indicated that **E4B9** indeed cross-reacts with human VE-cadherin (FIG. 6). This finding facilitates development of a "humanized" **E4B9** antibody and its success in the preclinical development since its anti-tumor activity can be tested extensively in several mouse models.

DETD . . . ELISA to determine the epitope domains for each monoclonal antibody. Fine epitope mapping of the three functional blocking monoclonal antibodies (**E4B9**, 19E6 and 10 G4) were made. The preliminary results showed that 19E6 and 10G4 recognize regions different from that of monoclonal antibody **E4B9** (FIGS. 7-9).

DETD [0096] Antibody **E4B9** inhibits new junction formation without disrupting existing junctions whereas other antibodies (19E6, 10G4 and Cad-5) disrupt existing junctions. During the. . . from the same cells (strand dimers) first and then from the opposing cells (adhesion dimers). Therefore, an antibody (such as **E4B9**) that antagonizes the "strand dimer" formation is sufficient to inhibit new junction formation. In contrast, disruption of the existing junctions. . .

CLM What is claimed is:

7. The antibody or antibody fragment of claim 1, wherein said monoclonal antibody is murine monoclonal antibody **E4B9**.

L4 ANSWER 3 OF 11 PCTFULL COPYRIGHT 2004 Univentio on STN

AN 2001075109 PCTFULL ED 20020822

TIEN ANTAGONIST ANTIBODIES TO VE-CADHERIN WITHOUT ADVERSE EFFECTS ON VASCULAR PERMEABILITY

TIFR ANTAGONISTES D'ANTICORPS DE LA VE-CADHERINE N'AYANT PAS D'EFFETS DEFAVORABLES SUR LA PERMEABILITE VASCULAIRE

IN LIAO, Fang;
HICKLIN, Daniel, J.;
BOHLEN, Peter

PA IMCLONE SYSTEMS INCORPORATED;
LIAO, Fang;
HICKLIN, Daniel, J.;
BOHLEN, Peter

DT Patent

PI WO 2001075109 A2 20011011

DS W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX
MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA

UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW
AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB
GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG

AI WO 2001-US10505 A 20010330
PRAI US 2000-09/540,967 20000331

ABEN This invention relates to antibodies, or immunologically active fragments thereof, specific for the N-terminal 15 amino acids of a mammalian VE-cadherin and which act as antagonists of VE-cadherin-mediated homophilic interactions between adjacent endothelial cells without adversely affecting normal vasculature. In a preferred embodiment, the antibodies are humanized antibodies directed that react with human VE-cadherin for use in a human. The invention also provides pharmaceutical compositions comprising these antibodies and antibody fragments, methods of preparing the antibodies, and methods of using the antibodies and antibody fragments to inhibit angiogenesis, inhibit tumor metastasis, or treat cell proliferative disorders.

ABFR L'invention concerne des anticorps ou des fragments a activite immunologique de ces anticorps, lesquels anticorps et fragments sont specifiques des acides amines 15 N-terminaux de la VE-cadherine d'un mammifere et agissent comme antagonistes d'interactions homophiles induites par la VE-cadherine entre des cellules endotheliales adjacentes sans avoir d'effets defavorables sur le systeme vasculaire. Dans un mode de realisation prefere, ces anticorps sont des anticorps humanises et diriges qui reagissent avec la VE-cadherine humaine afin d'etre utilises sur un etre humain. L'invention concerne egalement des compositions pharmaceutiques comprenant ces anticorps et ces fragments d'anticorps, des procedes de preparation et d'utilisation de ces anticorps et de ces fragments d'anticorps afin d'inhiber l'angiogenese et la metastase tumorale ou de traiter les troubles de la proliferation cellulaire.

DETD . . . FIG
FIG. 9: Predicted epitope region for antibody 19E6 and IOG4. The underlined
1 5 regions are the epitopes for antibodies **E4B9** and Cad-5, respectively.
. . .
as ect of the invention includes the hybridomas which produce
p
monoclonal antibodies of the invention. One such hybridorna producing rat anti-murine
VE-cadherin **E4B9** has been deposited with the ATCC, Rockville, Maryland and assigned
accession number
Techniques described for the production of single chain antibodies (U.S.. . .
. . .
+
I 0 TEA Domain 4 + +
Hecl.2 Domain 4
Anti-murine VEC
Toxicity
1 5 19E6 Domain 1 + + + + + + +
E4B9 Domain I + / - + + +
IOG4 Domain I ND + + + ND
6Dl0 Domain 3-4 + +
'See Table. . .

. . .
presumably from the same cells (strand dimers) first and then from the opposing cells (adhesion dimers). Therefore, an antibody (such as **E4B9**) that
antagonizes the strand dimer formation is sufficient to inhibit newjunction formation.

CLMEN 7 The antibody or antibody fragment of Claim 1, wherein said monoclonal antibody is murine monoclonal antibody **E4B9**.

L4 ANSWER 4 OF 11 IMSDRUGNEWS COPYRIGHT 2004 IMSWORLD on STN

AN 2000:1283 IMSDRUGNEWS
TI VE-cadherin-2 antagonists, ImClone Systems ImClone Systems preclinical data
SO R&D Focus Drug News (17 Apr 2000).
WC 94
TX At . . . to identify monoclonal antibody antagonists of vascular endothelial cadherin, with potential use in the treatment of cancer. The monoclonal antibody **E4B9** inhibited adherens junction formation with negligible disruption of existing junctions in vitro. The antibody also demonstrated the ability to block. . .

CN VE-cadherin-2 antagonists, ImClone Systems; **E4B9**

L4 ANSWER 5 OF 11 IMSDRUGNEWS COPYRIGHT 2004 IMSWORLD on STN

AN 97:4074 IMSDRUGNEWS
TI VE-cadherin-2 antagonists, ImClone Systems ImClone Systems targets tumor angiogenesis
SO R&D Focus Drug News (17 Nov 1997).
WC 90

CN VE-cadherin-2 antagonists, ImClone Systems; **E4B9**

L4 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:100430 BIOSIS
DN PREV200100100430
TI VE-Cadherin, a novel and specific target for anti-angiogenesis therapy.
AU Liao, F. [Reprint author]; Doody, J. F. [Reprint author]; Zanetta, L.; Wu, Y. [Reprint author]; Balderes, P. [Reprint author]; Li, Y. [Reprint author]; Dejana, E.; Mignatti, P.; Hicklin, D. J. [Reprint author]; Bohlen, P. [Reprint author]
CS ImClone Systems, Inc., New York, NY, USA
SO Journal of Submicroscopic Cytology and Pathology, (July, 2000) Vol. 32, No. 3, pp. 386. print.
Meeting Info.: XIth International Vascular Biology Meeting. Geneva, Switzerland. September 05-09, 2000.
ISSN: 1122-9497.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 21 Feb 2001
Last Updated on STN: 15 Feb 2002
IT . . .
Parts, Structures, & Systems of Organisms
cornea: sensory system

IT Diseases
tumor: neoplastic disease, treatment
Neoplasms (MeSH)
IT Chemicals & Biochemicals
E4B9: angiogenesis inhibitor, efficacy, toxicity; VE-cadherin [VEC]: angiogenic inhibitor, endothelial cell-specific cadherin

L4 ANSWER 7 OF 11 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
AN 2002-02757 BIOTECHDS
TI New antibody antagonists of VE-cadherin, which does not adversely affect vascular permeability, useful for inhibiting angiogenesis or tumor metastasis, e.g. autoimmune disease, carcinomas or leukemia tumors; vector-mediated gene transfer and expression in mammal cell, hybridoma cell culture for mouse monoclonal antibody production and transgenic animal for gene therapy
AU Liao F; Hicklin D J; Bohlen P
PA ImClone-Syst.
LO New York, NY, USA.
PI WO 2001075109 11 Oct 2001
AI WO 2001-US10505 30 Mar 2001
PRAI US 2000-540967 31 Mar 2000
DT Patent
LA English
OS WPI: 2001-656988 [75]
AB A mouse single chain monoclonal antibody (I, **E4B9**) or an antibody fragment, capable of binding to a VE-cadherin is claimed. Also claimed are: a hybridoma cell culture for the production of (I); a pharmaceutical composition containing (I); inhibition of angiogenesis or tumor metastasis in a mammal; an isolated nucleic acid with a DNA sequence that encodes for the antibody fragment, for a variable region of the antibody or for a hypervariable region of (I); an expression vector containing the nucleic acid; and administering the nucleic acid to a mammal to inhibit angiogeneiss or tumor neovascularization for gene therapy. Also disclosed as new are transgenic animals that express humanized antibodies. In an example, Lewis rats were immunized with a mixture of 4 KLH-coupled peptides with sequences from mouse VE-cadherin. Resulting hybridoma cells were produced for the production of (I). The above can be used for inhibiting angiogenesis associated with a neoplastic disease, an autoimmune disease, rheumatoid arthritis, diabetic retinopathy etc. or tumor metastasis e.g. carcinomas, gliomas, adenocarcinomas, lymphoid tumors etc. or for cell proliferative disorders. (44pp)
AB A mouse single chain monoclonal antibody (I, **E4B9**) or an antibody fragment, capable of binding to a VE-cadherin is claimed. Also claimed are: a hybridoma cell culture for. . .
CT VE-CADHERIN-SPECIFIC MOUSE RECOMBINANT SINGLE CHAIN MONOCLONAL ANTIBODY **E4B9** PREP., RAT HYBRIDOMA CELL CULTURE, VECTOR-MEDIATED GENE TRANSFER, EXPRESSION IN MAMMAL CELL, TRANSGENIC ANIMAL, HUMANIZED ANTIBODY, ANGIOGENESIS, CELL PROLIFERATIVE DISORDER,. . .

L4 ANSWER 8 OF 11 IFIPAT COPYRIGHT 2004 IFI on STN
AN 10216296 IFIPAT;IFIUDB;IFICDB
TI ANTIBODY ANTAGONISTS OF VE-CADHERIN WITHOUT ADVERSE EFFECTS ON VASCULAR PERMEABILITY; TO INHIBIT ANGIOGENESIS, INHIBIT TUMOR METASTASIS, OR TREAT CELL PROLIFERATIVE DISORDERS
INF Bohlen; Peter, New York, NY, US
Hicklin; Daniel J., Glen Ridge, NJ, US

Liao; Fang, New York, NY, US
IN Bohlen Peter; Hicklin Daniel J; Liao Fang
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG KENYON & KENYON, ONE BROADWAY, NEW YORK, NY, 10004, US
PI US 2002160003 A1 20021031
AI US 2002-40128 20020102
RLI US 2000-540967 20000331 CONTINUATION ABANDONED
FI US 2002160003 20021031
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 22
GI 9 Figure(s).

FIG. 1: VE-cadherin Dimerization. Two forms of VE-cadherin dimers are proposed based on the crystal structures resolved for N-and E-cadherins. The "strand dimer" (left panels) refers to homophilic interactions between two VE-cadherin molecules on the surface of the same cell. The "adhesion dimer" (right panels) refers to homophilic interactions between VE-cadherin molecules located on opposing cells.

FIG. 2: Sequence Alignment of ECD 1 of Four Classic Cadherins. Four regions of domain 1 for VE-cadherin are predicted to encompass the binding surface of either the strand dimer or the adhesion dimer. Four peptides (lower panels) are synthesized that encompass these regions to generate specific antibody inhibitors. Peptides 1: DEIWNQMHIDEEKNE-Cys; 2: YVKDQSNYNRQNAKYCys; 3: KYVLQGEFAGKIFGVDA-Cys and 4: LIVDKNTNKNLEQP-Cys. These peptides are represented by SEQ ID NOS. 1 and 4-6, respectively. The cysteine residue was added at the carboxyl end of each peptide for KLH-coupling.

FIG. 3:. Effects of the anti-ECD 1 (extracellular domain) peptides antibodies on paracellular permeability of H5V cells.

FIG. 4: Antibody **E4B9** does not exhibit significant effect on paracellular permeability. Antibodies **E4B9** and 6D 10 do not exert dramatic effect on vascular permeability.

FIGS. 5A & 5B: Antibody **E4B9** exhibits potent anti-angiogenesis activity in mouse corneal micropocket assay. Three representative eyes from each experimental group (6 mice/group) are tested. Antibody **E4B9** possesses greater-than 80% inhibitory activity on corneal neovascularization.

FIG. 6: Antibody **E4B9** cross-reacts with human VE-cadherin.

FIG. 7: Epitope mapping of new monoclonal antibodies. Strategy for mapping the epitope of m Ab 19E6 and 6D10.

FIG. 8: Summary of the epitope information for anti-ECD1 peptide antibodies. Antibody 10G4 epitope was mapped to the domain 1 of mouse VE-cadherin using the same strategy as previously described in FIG. 7.

FIG. 9: Predicted epitope region for antibody 19E6 and 10G4. The underlined regions are the epitopes for antibodies **E4B9** and Cad5, respectively.

AB This invention relates to antibodies, or immunologically active fragments thereof, specific for the N-terminal 15 amino acids of a mammalian VE-cadherin and which act as antagonists of VEcadherin-mediated homophilic interactions between adjacent endothelial cells without adversely affecting normal vasculature. In a preferred embodiment, the antibodies are humanized antibodies directed that react with human VE-cadherin for use in a human. The invention also provides pharmaceutical compositions comprising these antibodies and antibody fragments, methods of preparing the antibodies, and methods of using the

antibodies and antibody fragments to inhibit angiogenesis, inhibit tumor metastasis, or treat cell proliferative disorders.

GI . . .
FIG. 3:. Effects of the anti-ECD 1 (extracellular domain) peptides antibodies on paracellular permeability of H5V cells.
FIG. 4: Antibody **E4B9** does not exhibit significant effect on paracellular permeability. Antibodies **E4B9** and 6D 10 do not exert dramatic effect on vascular permeability.
FIGS. 5A & 5B: Antibody **E4B9** exhibits potent anti-angiogenesis activity in mouse corneal micropocket assay. Three representative eyes from each experimental group (6 mice/group) are tested. Antibody **E4B9** possesses greater-than 80% inhibitory activity on corneal neovascularization.
FIG. 6: Antibody **E4B9** cross-reacts with human VE-cadherin.
FIG. 7: Epitope mapping of new monoclonal antibodies. Strategy for mapping the epitope of m Ab. . . FIG. 7.
FIG. 9: Predicted epitope region for antibody 19E6 and 10G4. The underlined regions are the epitopes for antibodies **E4B9** and Cad5, respectively.

ACLM 7. The antibody or antibody fragment of claim 1, wherein said monoclonal antibody is murine monoclonal antibody **E4B9**.

L4 ANSWER 9 OF 11 PHIN COPYRIGHT 2004 PJB on STN

AN 2000:8218 PHIN
DN S00663074
DED 28 Apr 2000
TI PHARMAPROJECTS - New Biotechnology Products for week ending 28 April 2000
SO Scrip-Online-plus (2000)
DT Newsletter
FS FULL
TX

Recombinant vaccine (T2B)

Product Name	Originator
TBV25H	NIH
immunity vaccine, BioQuest	BioQuest

Recombinants, other (T2Z)

Product Name	Originator
rViscumin	Madaus

Monoclonal antibody, chimaeric (T3A4)

Product Name	Originator
WX-G250	Wilex Biotechnology

Monoclonal antibody, other (T3A9)

Product Name	Originator
E4B9	ImClone Systems
RED-103004	XiMed

Immunoconjugate, other (T3B9)

Product Name	Originator
5E10 MAb, IDEC	IDEC

Gene therapy (T4A)

Product Name	Originator
p53 gene ther, LP, Introgen	Introgen Therapeutics
prostate cancer vaccine, Vical	Vical
cancer vaccine,Antigen Express	Antigen Express

Antisense therapy (T4B)

Product Name	Originator
oligonucleotide 4625, Novartis	Novartis

Genomics technology (T4C)

Product Name	Originator
Pharmaprojects No. 6458	Genset

Biotechnology, other (T5Z)

Product Name	Originator
PNA anti-infectives, Pantheco	Pantheco

L4 ANSWER 10 OF 11 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 2001:56142 TOXCENTER
CP Copyright 2004 BIOSIS
DN PREV200100100430
TI VE-Cadherin, a novel and specific target for anti-angiogenesis therapy
AU Liao, F. [Reprint author]; Doody, J. F. [Reprint author]; Zanetta, L.; Wu, Y. [Reprint author]; Balderes, P. [Reprint author]; Li, Y. [Reprint author]; Dejana, E.; Mignatti, P.; Hicklin, D. J. [Reprint author]; Bohlen, P. [Reprint author]
CS ImClone Systems, Inc., New York, NY, USA
SO Journal of Submicroscopic Cytology and Pathology, (July, 2000) Vol. 32, No. 3, pp. 386. print.
Meeting Info.: XIth International Vascular Biology Meeting Geneva, Switzerland September 05-09, 2000
ISSN: 1122-9497.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
FS BIOSIS
OS BIOSIS 2001:100430
LA English
ED Entered STN: 20011116
Last Updated on STN: 20020219
ST . . .

Parts, Structures, & Systems of Organisms
cornea: sensory system
ST Diseases
tumor: neoplastic disease, treatment
Neoplasms (MeSH)
ST Chemicals & Biochemicals
E4B9: angiogenesis inhibitor, efficacy, toxicity; VE-cadherin [VEC]: angiogenic inhibitor, endothelial cell-specific cadherin
ST Methods & Equipment
anti-angiogenesis therapy: therapeutic method
ST . .

L4 ANSWER 11 OF 11 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-656988 [75] WPIDS
DNC C2001-193328
TI New antibody antagonists of VE-cadherin, which does not adversely affect vascular permeability, useful for inhibiting angiogenesis or tumor metastasis, e.g. autoimmune disease, carcinomas or leukemic tumors.
DC B04 D16
IN BOHLEN, P; HICKLIN, D J; LIAO, F
PA (IMCL-N) IMCLONE SYSTEMS INC; (BOHL-I) BOHLEN P; (HICK-I) HICKLIN D J; (LIAO-I) LIAO F
CYC 95
PI WO 2001075109 A2 20011011 (200175)* EN 44
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001049737 A 20011015 (200209)
US 2002160003 A1 20021031 (200274)
EP 1268799 A2 20030102 (200310) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003529370 W 20031007 (200370) 48
ADT WO 2001075109 A2 WO 2001-US10505 20010330; AU 2001049737 A AU 2001-49737 20010330; US 2002160003 A1 Cont of US 2000-540967 20000331, US 2002-40128 20020102; EP 1268799 A2 EP 2001-922997 20010330, WO 2001-US10505 20010330; JP 2003529370 W JP 2001-572983 20010330, WO 2001-US10505 20010330
FDT AU 2001049737 A Based on WO 2001075109; EP 1268799 A2 Based on WO 2001075109; JP 2003529370 W Based on WO 2001075109
PRAI US 2000-540967 20000331; US 2002-40128 20020102
AB WO 200175109 A UPAB: 20011220
NOVELTY - An antibody or an antibody fragment, capable of specifically binding to a VE-cadherin, and of inhibiting VE-cadherin mediated adherens junction formation in vitro but does not exert any significant or substantial effect on paracellular permeability in vitro, is new.

DETAILED DESCRIPTION - The antibody or an antibody fragment is capable of specifically binding to any one of the following groups:

(a) a site on a VE-cadherin, the site being within the 15 N-terminal amino acids of domain 1 of a VE-cadherin; and

(b) a site on a VE-cadherin, the site being within the 15 N-terminal amino acids of domain 1 of a VE-cadherin and the N-terminal amino acids having an insertion, deletion or substitution of 1-5 amino acids relative to a native VE-cadherin amino acid sequence;

(c) a peptide having an amino acid sequence: DEIWNQMHIDEEKNE (I);

(d) a peptide having an amino acid sequence: DWIWNQMHIDEEKNE (II); or
(e) a peptide having an amino acid sequence: DWIWNQMHIDEEKNT (III).
INDEPENDENT CLAIMS are also included for the following:
(1) a hybridoma, which produces the monoclonal antibodies;
(2) a pharmaceutical composition comprising the antibody or antibody fragment, and a pharmaceutical carrier or diluent;
(3) inhibiting angiogenesis in a mammal by administering the pharmaceutical composition to the mammal for a time and in an amount effective to inhibit angiogenesis;
(4) inhibiting tumor metastasis in a mammal by administering the pharmaceutical composition to the mammal for a time and in an amount effective to inhibit metastasis of a tumor;
(5) treating a cell proliferation disorder associated with vascularization in a mammal by administering the pharmaceutical composition to the mammal in an amount effective to inhibit proliferation of endothelial cells without disturbing the normal vasculature;
(6) reducing or inhibiting tumor vasculature in a mammal by administering the pharmaceutical composition to the mammal in an amount effective blood vessel formation without adversely affecting existing vasculature;
(7) an isolated nucleic acid comprising a nucleotide sequence, which encodes a coding sequence for the antibody fragment, for a variable region of the antibody or for a hypervariable region of the antibody cited above;
(8) an expression vector comprising the nucleic acid operably linked to sequences to control expression of the nucleotide sequence; and
(9) gene therapy which comprises administering the nucleic acid to a mammal in an amount and for a time to inhibit angiogenesis at a predetermined site or to inhibit tumor neovascularization.
ACTIVITY - Cytostatic; immunosuppressive; anti-inflammatory; ophthalmological. No test details given.
MECHANISM OF ACTION - VE-cadherin antagonist; angiogenesis inhibitor; gene therapy. No biological data was provided.
USE - The composition or the antibody (or antibody fragment) is useful for inhibiting angiogenesis (e.g. angiogenesis that is associated with a neoplastic disease, a solid tumor, an autoimmune disease, collagenous vascular disease, rheumatoid arthritis, an ophthalmological condition, diabetic retinopathy, retrolental fibroplasia or neovascular glaucoma), or tumor metastasis (e.g. carcinomas, gliomas, sarcomas, adenocarcinomas, adenosarcomas, adenomas, leukemic tumors or lymphoid tumors). The composition or antibody is also useful for treating a cell proliferation disorder associated with vascularization (e.g. blood vessel proliferation disorders, fibrotic disorders, angiogenesis, tumor growth, tumor metastasis, rheumatoid arthritis or age-related muscular degeneration). These may also be used for reducing or inhibiting tumor vasculature in a mammal. The nucleic acid that encodes the antibody or antibody fragment is useful in gene therapy, particularly for inhibiting angiogenesis or tumor neovascularization (claimed).
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TECH. . .
a monoclonal antibody or the antibody fragment is from a monoclonal antibody. Preferably, the monoclonal antibody is murine monoclonal antibody **E4B9**. The antibody or antibody fragment is preferably a single chain antibody, is humanized, is chimerized or is bispecific. The antibody. . .